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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/669,051	09/24/2000	Nicolas F. Franano	55225	2612

7590 08/12/2005

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EXAMINER

SRIVASTAVA, KAILASH C

ART UNIT

PAPER NUMBER

1655

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/669,051	FRANANO, NICOLAS F.
	Examiner	Art Unit
	Dr. Kailash C. Srivastava	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 17 May 2005.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 56,57,60-63,65-68 and 70-78 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 56,57,60-63, 65-68 and 70-78 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>17-05-2005</u>	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

DETAILED ACTION

1. The Art Unit Location to which your application has been assigned at the USPTO is changed to Art Unit 1655. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Kailash C. Srivastava in Art Unit 1655.
2. Applicant's response and amendment filed 17 May 2005 to Office Action mailed 17 November 2004 is acknowledged and entered. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office action.
3. Applicant's Declaration filed under 37 C.F.R §1.132 on 17 May 2005 is acknowledged and entered.

CLAIMS STATUS

4. Claims 1-55, 58-59, 64 and 69 are cancelled.
5. Claims 70-78 have been added.
6. Claims 56-57, 60-63 and 65-68 have been amended.
7. Claims 56-57, 60-63, 65-68 and 70-78 are pending and are examined on merits.

Information Disclosure Statement

8. Applicant's Supplemental Information Disclosure filed 17 May 2005 has been made of record and considered.

Objection to Specification

9. The amendment filed 17 May 2005 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure for e.g., is as follows:

- At Page 6, Line 8 of the amendment filed 5/17/2005, the phrase "at least about 20%".
- At Page 4, Line 13 of the amendment filed 5/17/2005, the word "targets" replaced with the originally filed recitation, "agents".

Applicant is required to cancel all recitations of the new matter in the reply to this Office Action.

Claim Rejections - 35 U.S.C. § 112

First Paragraph Rejections

10. In view of applicant's amendment, argument and Declaration less than 37 C.F.R §1.132 filed 17 May 2005, Examiner herewith withdraws the enablement and scope rejections to Claims 56-69 under 35 U.S.C. § 112, First Paragraph to Claims 56-69 in Office Action mailed 17 November 2004.

Second Paragraph Rejections

11. Pursuant to the amendments made, and arguments presented in applicant's amendment filed 17 May 2005, the Examiner hereby withdraws rejections made under 35 U.S.C. § 112 ¶2 to Claims 56-69 in Office Action mailed 17 November 2004.

12. In view of applicants' amendment filed 17 May 2005, following are new rejections to Claims 67-68 and 78 under 35 U.S.C. §112, second paragraph.

13. Claims 67-68 and newly filed Claim 78 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Recitation, "isolated" renders Claim 67 vague and unclear. Said recitation, in its present form does not define its metes and bounds. It is not clear whether said recitation means something removed from its original place or is referring to a remote or unique situation or what? Appropriate correction is required.
- Recitation, "selected" in Claim 68 is similar to the word "preferably" and is indefinite because it is not clear how one can determine with clarity and accuracy when and by whom the "selection" is to be exercised and what are the metes and bounds of said recitation.
- Claim 78 is rejected as being in improper form because a multiple dependent claim should refer to other claims in the alternative only, and can not depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, Claim 78 have not been further treated on the merits.

Claim Rejections – 35 U.S.C. § 102

14. In view of applicant's amendment, argument and Declaration under 37 C.F.R §1.132 filed 17 May 2005, Examiner herewith withdraws the anticipation rejection to Claims 56-69 under 35 U.S.C. § 102 (b)

to Claims 56, 59-63 and 67-68 as anticipated by Wolinsky et al. (U.S. Patent 4,636, 195) in Office Action mailed 17 November 2004.

15. In response to rejections under 35 U.S.C. § 102(a) to Claims 56-63, 65 and 67-68 as anticipatory by Dev et al. (U.S. Patent 5,944,710 in Office Action mailed 17 November 2004, citing Maillard et al. (Gene Therapy, 1998, Volume 5, Pages 1023-130) a reference that the applicant previously cited on USPTO 1449 applicant argues that Dev et al " does not teach or suggest enlarging the diameter of an artery or vein and fails to teach or suggest administering elastase in a dose sufficient to cause such enlargement because according to Maillard et al. a low elastase dose treatment of artery may cause aneurism and furthermore pre-incubation of internal elastic lamina is also applicable to permeate penetration of nucleic acid vectors. Applicant also cites another reference, Dev et al. U.S. Patent 6,347, 247 B1, Issued 2002 on an application filed on May 7, 1999 and argue that in this latter reference Dev et al., teach a different mechanism than that claimed in the instantly claimed application.

Applicants' arguments filed 17 May 2005 and cited *supra* regarding the rejections to Claims 56-63, 65 and 67-68 as anticipatory by Dev et al. (U.S. Patent 5,944,710 in Office Action mailed 17 November 2004 have been fully and carefully considered but are not persuasive for the reasons of record at pages 7-8, item 18 in the Office Action mailed 17 November 2004. This is because (i) Dev et al. Patent 6,347,247 B1 issued in 2002, even though filed on 7 May, 1999 does not anticipate applicants claimed invention under 35 U.S. C. 102 (a). (ii) Dev et al. similar to applicants are silent to an elastase dosage to be effective in de-obstructing an obstructed artery or vein according to the claimed invention and (ii) applicant's recited reference- Maillard et al. method does not claim to de-obstruct an obstructed artery or vein. Further reasons that applicants' arguments are not found persuasive are discussed *infra*.

Feit et al. (2003, J. Pat. Trade. Off. Soc., Vol. 85, No. 1, pages 5-21) teach three criteria for inherency. (1) The most important criterion is certainty. Citing *In re Tomlinson* and *In re Zierden*, Feit et al. state that certainty is established when the reference process necessarily results in the claimed process as opposed to a possibility. (2) The second criterion is chronology; it will always happen. Feit et al. state that the chronological test is forward chronology. Citing *Eli Lilly and Co. v Barr Laboratories, Inc.*, Feit et al. argue that the claimed result must always be obtained based upon the prior art method. 3) The third criterion is the legal standard. Feit et al., citing *Continental Can*, state that the legal standard is whether the missing descriptive material would be so recognized by a person of ordinary skill in the art as necessarily present in the thing.

With reference to anticipation rejections cited *supra*, the first of Feit et al's teachings is met because the compositions that Dev et al. teach comprises the same components (i.e., elastase). Since, in said method de-obstructs arteries and cardiovascular restenosis via local intravascular delivery through a catheter to the endothelial lining of a blood vessel in to a subject, said method inherently accomplishes

the same end result as claimed in the instant application. Therefore, it satisfies the first criterion as taught by Feit et al. The second and third teachings from Feit et al., logically follow because the first teaching is met by the cited prior art reference (i.e., Dev et al., U. S. Patent 5,944,710).

16. The following new rejection is made in view of applicant's above-cited amendments.
17. Amended Claims 56, 60-61, 65 and 67 rejected under 35 U.S.C. §102(b) as anticipated by Bini (U.S. Patent 5,922,322).

Claims recite a method comprising local administration to the wall of an artery or vein in a human subject a composition comprising elastase to treat an artery or vein in a human subject, wherein the artery or vein is obstructed. Said administration "results in proteolysis of elastin in the wall of the artery or vein leading to enlargement of the diameter of the artery or vein". The method further comprises administering said composition by a catheter, said obstruction being coronary obstruction.

Bini teaches a method to treat arteriosclerotic plaque via injecting through a catheter a matrix metalloprotease (i.e., MMP), wherein said MMP are one of MMP-2 and MMP-9 having an elastase activity and they hydrolyse/ break down a number of proteins e.g., collagen and elastin that are associated with extracellular matrix (Column 3, Lines 15-25; Column 5, Lines 38-40 and Lines 20-30). Note that the prior art method teaches administering the same enzyme (i.e., elastase) according the same step (i.e., via injecting through a catheter) to the same organ (i.e., arterial cell wall) to treat the same condition (i.e., plaque of the) .e., extracellular matrix that inherently causes arterial or venous obstruction). Thus, the prior art inherently, teaches a method to alleviate arterial obstruction in a human patient via injecting into the arterial wall an elastase composition through a catheter. Furthermore, Bini teaches a certain elastase dosage to be injected to dislodge the plaque and therefore administering said dosage to said subject would inherently function in the same way as claimed instantly because, same composition is being administered through same apparatus and is alleviating the same problem (i.e., arterial blockage) as is recited in the claimed invention. Therefore, the prior art method inherently must function as instantly claimed (See e.g., In re Best, 195 USPQ 430, 433-CCPA 1977).

Therefore, the reference deems to anticipate claims 26, 30-31 and 34-35.

Claim Rejections Under 35 U.S.C. § 103(a)

18. In view of applicant's amendment, argument and Declaration under 37 C.F.R §1.132 filed 17 May 2005, Examiner herewith withdraws the rejection to Claims 56-69 under 35 U.S.C. § 103 (a) as obvious over Wolinsky (U.S. Patent 4,636,195) in view of Dev et al (U.S. Patent 5, 944,710).
19. In view of applicant's amendment filed 17 May 2005, following is a new rejection under 35 U.S.C. §103(a) to Claims 56-57, 60-63, 65-68 and newly presented Claims 70-78.

20. Claims 56-57, 60-63, 65-68 and newly presented Claims 70-78 are rejected under 35 U.S.C. § 103 (a) as being obvious/unpatentable over Bini (U.S. Patent 5,922,322) in view of Dev et al (U.S. Patent 5, 944,710) for the reasons of record at pages 9-10 in Office Action mailed May 17 2005 and for additional reasons as discussed *infra*.

Claims recite a method comprising local administration to the wall of an artery or vein in a human subject a composition comprising elastase to de-obstruct an artery or vein in a human subject, wherein the artery or vein is obstructed. Said administration "results in proteolysis of elastin in the wall of the artery or vein leading to enlargement of the diameter of the artery or vein". The method further comprises administering said composition by a catheter, said obstruction being stenosis or coronary obstruction. Claims are also directed to administering said composition to "an isolated or selected segment of the artery or vein located within the human subject". Newly added claims 70-78 are dependent on previously rejected Claim 64, now cancelled.

Teachings from Bini have been discussed above. Bini, however, does not explicitly teach administering a composition comprising elastase, to the wall of a blood vessel to treat stenosis or other blood vessel obstructed diseases.

Dev et al. explicitly teach that a composition comprising elastase is administered to the cells of endothelial lining of a blood vessel via a catheter. Note that the endothelial lining of the blood vessel comprises the wall of a blood vessel. Furthermore, a blood vessel encompasses both an artery or a vein and any artery or vein. Thus, Dev et al. teach de-clogging an obstructed artery or a vein via injecting to the wall of said artery or vein a composition comprising elastase through a catheter and further teach applying said method for cardiologic applications (Column 3, Lines 34-45). Therefore, Dev et al. teach de-clogging vascular obstruction encompassing an artery or vein, stenosis, artery or vein connected to an arteriovenous hemodialysis graft, coronary obstruction or obstruction by intimal hyperplasia.

One having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from Bini according to teachings from Dev et al. to obtain a method to de-clog an obstructed blood vessel, wherein said clogging is stenosis, artery or vein connected to an arteriovenous hemodialysis graft, coronary obstruction or obstruction by intimal hyperplasia via delivering to the blood vessel wall a composition comprising elastase through a catheter, because each of the prior art references teach de-clogging a blood vessel and Dev et al. beneficially teach that said composition comprising elastase is delivered to vascular endothelial lining (i.e., vascular wall) and is applicable to cardiologic applications. Thus, Dev et al. remedy the deficiency of elastase and delivery to a vessel/ arterial/ venous wall a composition comprising elastase in Bini's teachings.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify/combine Bini's teachings with those from Dev et al. to obtain a method to

de-clog an obstructed blood vessel, wherein said clogging is stenosis, artery or vein connected to an arteriovenous hemodialysis graft, coronary obstruction or obstruction by intimal hyperplasia via delivering to the blood vessel wall a composition comprising elastase through a catheter. Dev et al. remedy the deficiency in Bini's teachings of elastase and delivery to a vessel/ arterial/ venous wall a composition comprising elastase. Instantly claimed arteriovenous hemodialysis graft, or obstruction by intimal hyperplasia is not explicitly taught in the cited prior arts. However, since the prior art teaches application of prior art method to a cardiologic application, the adjustment of particular conventional working conditions (e.g., application of instantly claimed method to a particular type of blood vessel obstruction) is deemed merely a matter of judicious selection and routine optimization of a result-effective parameter, which is well within the purview of the skilled artisan.

It would have been further obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings from Bini and Dev et al. for the known benefits of administering a composition comprising elastase to de-obstruct a blood vessel since it is well known in the art to administer a protease especially a collagenase or elastase for the same purpose (i.e., to de-obstruct an obstructed blood vessel and for the following reasons. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. Applicants invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any ingredient embraced by the claims that does not exhibit an unexpected result (e.g., synergism) is therefore *ipso facto* unpatentable.

Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above-cited references before him.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

CONCLUSION

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date

of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. For the aforementioned reasons, no claims are allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Bruce Campell, can be reached on (571)-272-0974 Monday through Friday 8:00 A.M. to 4:30 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.


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August 8, 2005


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